

### **REMARKS**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. Claim 1 has been amended to recite that R<sub>4</sub>, R<sub>5</sub> and R<sub>7</sub>, and R<sub>6</sub> include haloalkyl. This amendment is explicitly supported by the specification as follows:

“R<sub>4</sub>, R<sub>5</sub> and R<sub>7</sub> are independently selected from hydrogen, halogen, hydroxy, alkyl, (including cycloalkyl and haloalkyl (such as trifluoromethyl) and arylalkyl) . . .” (Page 8, lines 28-29). (Emphasis added).

“R<sub>6</sub> is selected from hydrogen, halogen, alkyl, (including cycloalkyl and haloalkyl (such as trifluoromethyl) and arylalkyl) . . .” (Page 9, lines 10-11). (Emphasis added).

### **Claim Objections**

Claim 1 has been amended to overcome the objection to claim 11. Applicants note that contrary to the wording of the office action, original claim 1 did explicitly include in the proviso “R<sub>5</sub> is selected from . . . haloalkyl” at the end of the claim. Moreover, as noted above, this amendment is explicitly supported in the specification.

### **Claim Rejections Under 35 USC 112**

Claim 1 has been amended to overcome the rejection to claim 1 for being indefinite.

### **Claim Rejections Under 35 USC 102**

Claims 1-14 were rejected for lack of novelty over Jonas et al., US 3,853,878. Applicants traverse this rejection for the following reasons. Claim 1 recites that “either at least one of R<sub>5</sub> and R<sub>6</sub> is Cl, F, haloalkyl or Br, or R<sub>5</sub> is halogen, haloalkyl or alkylthio”. None of these compounds are disclosed by Jonas, either explicitly or as intermediates. Therefore, Jonas cannot anticipate the present claims.

**Claim Rejections Under 35 USC 103**

Claims were rejected as being obvious over Moskrosz, Med. Chem. Res. 3:240-248, 1993 and Bos CA 2,097,465 in view of Moskrosz, Med. Chem. Res. 3:240-248, 1993. Applicants traverse these rejections for the following reasons.

In contrast to the present claims, Mokrosz discloses compounds without substituents on the phenyl ring. Applicants have attached a 132 Declaration evidencing that the claimed compounds possess superior potency compared to the compounds of Mokrosz. This is an unexpected result, which demonstrates that the present invention is not obvious over Mokrosz.

The structural difference of the presently claimed compounds over those of Bos is that the C-10 position in the presently claimed compounds is saturated whereas the compounds of Bos contain a double bond in this position.

Applicants contend that Mokrosz would not have motivated the skilled person to modify the compounds of Bos in a manner which would result in the presently claimed compounds, i.e. by saturating this double bond.

When one compares compounds (5) and (6) of Mokrosz, which both have an unsubstituted (-NH) group in the piperazine ring, it can be seen that the unsaturated compound (5) has a  $K_i$  (5HT<sub>2</sub>) of 1800nM whereas the saturated compound (6) has a higher  $K_i$  (5HT<sub>2</sub>) of 3570nM. In addition, when compounds (7) and (8) are compared, which both have an -N(Et) group in the piperazine ring, it can be seen that the unsaturated compound (8) has a  $K_i$  (5HT<sub>2</sub>) of 3610nM whereas the saturated compound (7) has a higher  $K_i$  (5HT<sub>2</sub>) of 3780nM. In both instances, therefore, the saturated compound has a higher  $K_i$  and is therefore less strongly binding than the unsaturated compound.

Accordingly, the skilled person would not be motivated to modify the compounds of Bos on the basis of Mokrosz because Mokrosz shows that removing the unsaturation leads to a reduction in the binding affinity. Thus, a combination of Bos and Mokrosz would not lead

the skilled person to the compounds set out in claim 1 of the present Application. Therefore the claimed subject-matter is, *prima facie*, nonobvious.

**Conclusion**

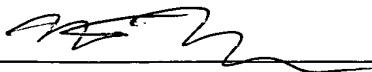
Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By  \_\_\_\_\_

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